

REC'D 19 DEC 2001

PCT

WIPO

PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference KLP/B45226	<b>FOR FURTHER ACTION</b>	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP00/09367	International filing date (day/month/year) 22/09/2000	Priority date (day/month/year) 24/09/1999
International Patent Classification (IPC) or national classification and IPC A61K9/00		
<p><b>Applicant</b> SMITHKLINE BEECHAM BIOLOGICALS S.A. et al.</p>		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 8 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I    <input checked="" type="checkbox"/> Basis of the report</li> <li>II   <input type="checkbox"/> Priority</li> <li>III   <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li>IV   <input type="checkbox"/> Lack of unity of invention</li> <li>V   <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI   <input type="checkbox"/> Certain documents cited</li> <li>VII   <input checked="" type="checkbox"/> Certain defects in the international application</li> <li>VIII   <input checked="" type="checkbox"/> Certain observations on the international application</li> </ul>		

Date of submission of the demand 20/04/2001	Date of completion of this report 17.12.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Hedegaard, A Telephone No. +49 89 2399 8644



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP00/09367

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):
- Description, pages:**

1-49                   as originally filed

**Claims, No.:**

1-32                   as originally filed

**Drawings, sheets:**

1/4-4/4               as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
  - the language of publication of the international application (under Rule 48.3(b)).
  - the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description,               pages:
- the claims,                   Nos.:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP00/09367

- the drawings, sheets:
5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):  
*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*
6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
- the entire international application.
- claims Nos. 23-26.
- because:
- the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for the said claims Nos. .
2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
- the written form has not been furnished or does not comply with the standard.
- the computer readable form has not been furnished or does not comply with the standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N) Yes: Claims 32

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP00/09367

No: Claims 1-31

Inventive step (IS) Yes: Claims

No: Claims 1-32

Industrial applicability (IA) Yes: Claims 1-22, 27-32

No: Claims

2. Citations and explanations  
see separate sheet

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:  
see separate sheet

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

---

International application No. PCT/EP00/09367

**R S ction III**

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claims 23-26 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

**Re Section V**

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

D1: WO-A-96 33738

D2: Derwent publications Ltd., London, GB; Class B04, AN 1998-167654 &  
RU 2 086 232

D3: WO-A-94 17827

D4: WO-A-99 52549

D1 discloses (see claim 1) an influenza virus vaccine formulation comprising an immunogenic amount of inactivated influenza virus. In a preferred embodiment, the vaccine is packaged in a single dosage for immunization by e.g. intranasal administration (see the paragraph bridging pages 22 and 23).

D2 discloses a composition for intra-nasal prevention based on inactivated influenza vaccine. The composition has prolonged action and produces a high immune response.

D3 discloses (see claims 1, 2 and 5) influenza virus antigen compositions for nasal administration comprising non-ionic surfactants.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP00/09367

D4 (see example 12) discloses a vaccine formulation for one-dose intranasal administration comprising inactivated influenza virus and non-ionic surfactant. On page 9, line 15 split influenza virus is disclosed.

2. The subject-matter of independent claims 1, 23 and 27 is not novel (Art. 33(2) PCT) over D1 and D2, each document taken separately (see above under item 1).

It is here pointed out that the parameters "international regulatory requirements" in claim 1 and "European Union criteria" in claim 23 are too unclear to be used as distinguishing features (see below in Section VIII, item 1).

3. The subject-matter of independent claim 32 is novel since the features "split" and "non-ionic surfactant" are not to be found in the documents D1 and D2 (see however below under item 5).

The use of "split vaccines" and "non-ionic surfactants" as defined in claim 32 is however well-known to the skilled person working in the field of influenza vaccines for nasal administration (see e.g. D3 (claim 1) and the present application, page 5, line 28). The skilled person would therefore regard it as a normal design option to include these features in the formulations according to D1 and/or D2 thereby arriving at a method according to the present claim 32. The subject-matter of claim 32 does therefore not appear to involve an inventive step (Article 33(3) PCT).

4. A positive international preliminary report for the subject-matter of the dependent claims 2-22, 24-26 and 28-31 can only be established when they refer to independent claims which meet the requirements of the PCT.
5. Although D4 (priority dates 09.04.98 and 25.09.98; filing date 29.03.99 and publication date 21.10.99) does not constitute prior art within the meaning of Rule 64.1(b) PCT, it could become of relevance for novelty in the regional phase since

disclosing all the features of present independent claims 1, 23, 27 and 32.

No check has been made as to whether the priorities have been validly claimed.

6. For the assessment of the present claims 23-26 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**Re Section VII**

Certain defects in the international application

1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1 and D2 is not mentioned in the description, nor are these documents identified therein.
2. The statement "incorporated herein by reference" used throughout the description is ambiguous and is not allowed in some national patent legislation (e.g. EPC).

**Re Section VIII**

Certain observations on the international application

1. Claims 1-3, 23-25 and 28 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claims attempt to define the subject-matter in terms of the result to be achieved which merely amounts to a statement of the underlying problem ("generates an immune

response which meets international regulatory requirements for influenza vaccines" and "achieves the European Union Criteria for seroconversion rate, seroprotection rate and seroconversion factor"). The technical features necessary for achieving these results should be added.

Furthermore, the features "international regulatory requirements for influenza vaccines" in claims 1 and 28 and " European Union criteria" in claims 2-3 could be subject to variations with time and render the definition of the subject-matter of these claims unclear (Article 6 PCT).

2. The word "about", particularly when applied to a range, detracts from the general clarity of the claims (Art. 6 PCT).
3. The term "low" used in claim 16 is vague and unclear and leaves the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of said claim unclear (Article 6 PCT).
4. The abbreviation "3D-MPL" in claims 21 and 22 should be clearly defined (Art. 6 PCT).

## PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION  
(PCT Rule 61.2)

Date of mailing (day/month/year) 16 August 2001 (16.08.01)	To:  Commissioner US Department of Commerce United States Patent and Trademark Office, PCT 2011 South Clark Place Room CP2/5C24 Arlington, VA 22202 ETATS-UNIS D'AMERIQUE  in its capacity as elected Office
International application No. PCT/EP00/09367	Applicant's or agent's file reference KLP/B45226
International filing date (day/month/year) 22 September 2000 (22.09.00)	Priority date (day/month/year) 24 September 1999 (24.09.99)
Applicant FRIEDE, Martin et al	

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

20 April 2001 (20.04.01)

in a notice effecting later election filed with the International Bureau on:

\_\_\_\_\_

2. The election  was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No.: (41-22) 740.14.35	Authorized officer  Juan Cruz  Telephone No.: (41-22) 338.83.38
---	---

## PARTNERSHIP COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

Date of mailing (day/month/year) 21 February 2002 (21.02.02)
Applicant's or agent's file reference KLP/B45226
International application No. PCT/EP00/09367

To:  
 PRIVETT, Kathryn, Louise  
 SmithKline Beecham  
 Corporate Intellectual Property  
 (CN9.25.1)  
 980 Great West Road  
 Brentford, Middlesex TW8 9GS  
 ROYAUME-UNI

## IMPORTANT NOTIFICATION

International filing date (day/month/year)  
22 September 2000 (22.09.00)

## 1. The following indications appeared on record concerning:

the applicant     the inventor     the agent     the common representative

Name and Address  PRIVETT, Kathryn, Louise Corporate Intellectual Property SmithKline Beecham Two New Horizons Court Brentford Middlesex TW8 9EP United Kingdom	State of Nationality	State of Residence
	Telephone No. +44 20 8975 2585	
	Facsimile No. +44 20 8975 6294	
	Teleprinter No.	

## 2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

the person     the name     the address     the nationality     the residence

Name and Address  PRIVETT, Kathryn, Louise SmithKline Beecham Corporate Intellectual Property (CN9.25.1) 980 Great West Road Brentford, Middlesex TW8 9GS United Kingdom	State of Nationality	State of Residence
	Telephone No. +44 20 8047 5000	
	Facsimile No. +44 20 8047 6894	
	Teleprinter No.	

## 3. Further observations, if necessary:

## 4. A copy of this notification has been sent to:

<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned
<input type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No.: (41-22) 740.14.35	Authorized officer  Dominique DELMAS  Telephone No.: (41-22) 338.83.38
---	--

## PENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>KLP/B45226</b>	<b>FOR FURTHER ACTION</b>	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. <b>PCT/EP 00/09367</b>	International filing date (day/month/year) <b>22/09/2000</b>	(Earliest) Priority Date (day/month/year) <b>24/09/1999</b>
Applicant <b>SMITHKLINE BEECHAM BIOLOGICALS S.A. et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
  - contained in the international application in written form.
  - filed together with the international application in computer readable form.
  - furnished subsequently to this Authority in written form.
  - furnished subsequently to this Authority in computer readable form.
  - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
  - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.  Certain claims were found unsearchable (See Box I).

3.  Unity of invention is lacking (see Box II).

4. With regard to the **title**,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

INTRANASAL INFLUENZA VIRUS VACCINE

5. With regard to the **abstract**,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. \_\_\_\_\_

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

None of the figures.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 00/09367

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 7 A61K9/00

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, EPO-Internal, CHEM ABS Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 96 33738 A (VOLVOVITZ, FRANKLIN) 31 October 1996 (1996-10-31)</p> <p>claims 1,2,5 page 22, line 36 -page 23, line 3 ---</p>	1-4, 12-19, 23-30
X	<p>DATABASE WPI Section Ch, Week 199815 Derwent Publications Ltd., London, GB; Class B04, AN 1998-167654 XP002158395 &amp; RU 2 086 232 A (UFA VACCINES) abstract ---</p> <p>-/-</p>	1-4, 23-30

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

25 January 2001

Date of mailing of the international search report

05/02/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Ventura Amat, A

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 00/09367

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 99 52549 A (SMITHKLINE BEECHAM) 21 October 1999 (1999-10-21)	1-8, 16-19, 23-32
P, Y	claims 1,2,10,13,23 page 9, line 1 -page 10, line 31 ---	6-11
P, X	WO 00 47222 A (BAXTER) 17 August 2000 (2000-08-17)	1-4, 12-19, 23-30
	claim 1 ---	
Y	WO 94 17827 A (LYFJATHROUN) 18 August 1994 (1994-08-18) claims 1,2,4,5 ---	6-8
Y	WO 96 36352 A (MODI, PANKAJ; ET AL.) 21 November 1996 (1996-11-21) claims 1,11 -----	6-11

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 00/09367

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9633738	A	31-10-1996	US	5976552 A	02-11-1999
			AU	696690 B	17-09-1998
			AU	5631296 A	18-11-1996
			AU	722699 B	10-08-2000
			AU	9715898 A	04-03-1999
			CA	2222283 A	31-10-1996
			EP	0830141 A	25-03-1998
RU 2086232	A	10-08-1997	NONE		
WO 9952549	A	21-10-1999	AU	3419799 A	01-11-1999
			EP	1069910 A	24-01-2001
WO 0047222	A	17-08-2000	AT	19499 A	15-12-2000
			AU	2525300 A	29-08-2000
WO 9417827	A	18-08-1994	AT	195077 T	15-08-2000
			AU	668290 B	26-04-1996
			AU	6106594 A	29-08-1994
			CA	2156084 A	18-08-1994
			DE	69425427 D	07-09-2000
			EP	0682528 A	22-11-1995
			ES	2150982 T	16-12-2000
			JP	9508614 T	02-09-1997
			NO	953182 A	12-10-1995
			US	5942237 A	24-08-1999
WO 9636352	A	21-11-1996	US	5653987 A	05-08-1997
			AU	5642396 A	29-11-1996
			CA	2210996 A	21-11-1996
			EP	0813421 A	29-12-1997

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:

CORPORATE INTELLECTUAL PROPERTY  
SMITHKline Beecham  
Attn. PRIVETT, Kathryn Louise  
Two New Horizons Court  
Brentford,  
Middlesex TW8 9EP  
UNITED KINGDOM

PCT

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT  
OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing  
(day/month/year)

05/02/2001

Applicant's or agent's file reference <b>KLP/B45226</b>	<b>FOR FURTHER ACTION</b> See paragraphs 1 and 4 below
International application No. <b>PCT/EP 00/09367</b>	International filing date (day/month/year) <b>22/09/2000</b>
Applicant <b>SMITHKLINE BEECHAM BIOLOGICALS S.A. et al.</b>	

1.  The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland  
Fascimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2.  The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3.  With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau.

If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority  European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer <b>Petronella Vaassen-Elsackers</b>
---	---

## NO TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

#### What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

#### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

**The amendments must be made in the language in which the international application is to be published.**

#### What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

**The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.**

## NOTES TO FORM PCT/ISA/220 (c) continued

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

**The following examples illustrate the manner in which amendments must be explained in the accompanying letter:**

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

### "Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

### Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

### Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

## PATENT COOPERATION TREATY

PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>KLP/B45226</b>	<b>FOR FURTHER ACTION</b>	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. <b>PCT/EP 00/09367</b>	International filing date (day/month/year) <b>22/09/2000</b>	(Earliest) Priority Date (day/month/year) <b>24/09/1999</b>
Applicant <b>SMITHKLINE BEECHAM BIOLOGICALS S.A. et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

- the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
- contained in the international application in written form.
  - filed together with the international application in computer readable form.
  - furnished subsequently to this Authority in written form.
  - furnished subsequently to this Authority in computer readable form.
  - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
  - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.  Certain claims were found unsearchable (See Box I).

3.  Unity of invention is lacking (see Box II).

4. With regard to the title,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

INTRANASAL INFLUENZA VIRUS VACCINE

5. With regard to the abstract,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

None of the figures.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP 00/09367

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  

Although claims 23-26 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 00/09367

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K9/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, EPO-Internal, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 33738 A (VOLVOVITZ, FRANKLIN) 31 October 1996 (1996-10-31)  claims 1,2,5 page 22, line 36 -page 23, line 3 ---	1-4, 12-19, 23-30
X	DATABASE WPI Section Ch, Week 199815 Derwent Publications Ltd., London, GB; Class B04, AN 1998-167654 XP002158395 & RU 2 086 232 A (UFA VACCINES) abstract --- -/-	1-4, 23-30

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

25 January 2001

Date of mailing of the international search report

05/02/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel: (+31-70) 340-2040, Tx. 31 651 epo nl.  
 Fax: (+31-70) 340-3016

Authorized officer

Ventura Amat, A

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 00/09367

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 99 52549 A (SMITHKLINE BEECHAM) 21 October 1999 (1999-10-21)	1-8, 16-19, 23-32
P,Y	claims 1,2,10,13,23 page 9, line 1 -page 10, line 31 ---	6-11
P,X	WO 00 47222 A (BAXTER) 17 August 2000 (2000-08-17)  claim 1 ---	1-4, 12-19, 23-30
Y	WO 94 17827 A (LYFJATHROUN) 18 August 1994 (1994-08-18) claims 1,2,4,5 ---	6-8
Y	WO 96 36352 A (MODI, PANKAJ; ET AL.) 21 November 1996 (1996-11-21) claims 1,11 -----	6-11

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 00/09367

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9633738 A	31-10-1996	US 5976552 A		02-11-1999
		AU 696690 B		17-09-1998
		AU 5631296 A		18-11-1996
		AU 722699 B		10-08-2000
		AU 9715898 A		04-03-1999
		CA 2222283 A		31-10-1996
		EP 0830141 A		25-03-1998
RU 2086232 A	10-08-1997	NONE		
WO 9952549 A	21-10-1999	AU 3419799 A		01-11-1999
		EP 1069910 A		24-01-2001
WO 0047222 A	17-08-2000	AT 19499 A		15-12-2000
		AU 2525300 A		29-08-2000
WO 9417827 A	18-08-1994	AT 195077 T		15-08-2000
		AU 668290 B		26-04-1996
		AU 6106594 A		29-08-1994
		CA 2156084 A		18-08-1994
		DE 69425427 D		07-09-2000
		EP 0682528 A		22-11-1995
		ES 2150982 T		16-12-2000
		JP 9508614 T		02-09-1997
		NO 953182 A		12-10-1995
		US 5942237 A		24-08-1999
WO 9636352 A	21-11-1996	US 5653987 A		05-08-1997
		AU 5642396 A		29-11-1996
		CA 2210996 A		21-11-1996
		EP 0813421 A		29-12-1997

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
29 March 2001 (29.03.2001)

PCT

(10) International Publication Number  
**WO 01/21151 A1**

(51) International Patent Classification<sup>7</sup>: **A61K 9/00**

[BE/BE]; SmithKline Beecham Biologicals s.a., Rue de l'Institut 89, B-1330 Rixensart (BE).

(21) International Application Number: **PCT/EP00/09367**

(74) Agent: **PRIVETT, Kathryn, Louise; Corporate Intellectual Property, SmithKline Beecham, Two New Horizons Court, Brentford, Middlesex TW8 9EP (GB).**

(22) International Filing Date:  
22 September 2000 (22.09.2000)

English

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

9922700.1 24 September 1999 (24.09.1999) GB  
9922703.5 24 September 1999 (24.09.1999) GB  
0016686.8 6 July 2000 (06.07.2000) GB

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant (*for all designated States except US*):  
**SMITHKLINE BEECHAM BIOLOGICALS S.A.**  
[BE/BE]; Rue de l'Institut 89, B-1330 Rixensart (BE).

Published:

- *With international search report.*
- *Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.*

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **FRIEDE, Martin** [GB/BE]; SmithKline Beecham Biologicals s.a., Rue de l'Institut 89, B-1330 Rixensart (BE). **HENDERICKX, Veronique** [BE/BE]; SmithKline Beecham Biologicals s.a., Rue de l'Institut 89, B-1330 Rixensart (BE). **HERMAND, Philippe** [BE/BE]; SmithKline Beecham Biologicals s.a., Rue de l'Institut 89, B-1330 Rixensart (BE). **SLAOUI, Moncef, Mohamed** [BE/BE]; SmithKline Beecham Biologicals s.a., Rue de l'Institut 89, B-1330 Rixensart (BE). **THOELEN, Stefan, Gabriel, Josef**

WO 01/21151 A1

(54) Title: INTRANASAL INFLUENZA VIRUS VACCINE

(57) Abstract: The invention relates to the use of a non-live influenza virus antigen preparation, particularly a split influenza virus preparation, in the manufacture of a vaccine formulation for a one-dose intranasal vaccination against influenza, wherein the one-dose vaccination meets international regulatory requirements for influenza vaccines. Further provided are methods for the production of the vaccine, and a pharmaceutical kit comprising an intranasal administration device and the one-dose vaccine.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 00/09367

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 7 A61K9/00

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, EPO-Internal, CHEM ABS Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 33738 A (VOLVOVITZ, FRANKLIN) 31 October 1996 (1996-10-31)  claims 1,2,5 page 22, line 36 -page 23, line 3 ---	1-4, 12-19, 23-30
X	DATABASE WPI Section Ch, Week 199815 Derwent Publications Ltd., London, GB; Class B04, AN 1998-167654 XP002158395 & RU 2 086 232 A (UFA VACCINES) abstract --- -/-	1-4, 23-30

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*8\* document member of the same patent family

Date of the actual completion of the international search

25 January 2001

Date of mailing of the international search report

05/02/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentbaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.  
Fax: (+31-70) 340-3016

Authorized officer

Ventura Amat, A

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP 00/09367

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 99 52549 A (SMITHKLINE BEECHAM) 21 October 1999 (1999-10-21)	1-8, 16-19, 23-32
P, Y	claims 1,2,10,13,23 page 9, line 1 -page 10, line 31 ---	6-11
P, X	WO 00 47222 A (BAXTER) 17 August 2000 (2000-08-17)	1-4, 12-19, 23-30
	claim 1 ---	
Y	WO 94 17827 A (LYFJATHROUN) 18 August 1994 (1994-08-18) claims 1,2,4,5 ---	6-8
Y	WO 96 36352 A (MODI, PANKAJ; ET AL.) 21 November 1996 (1996-11-21) claims 1,11 -----	6-11

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 00/09367

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 9633738	A	31-10-1996		US 5976552 A AU 696690 B AU 5631296 A AU 722699 B AU 9715898 A CA 2222283 A EP 0830141 A		02-11-1999 17-09-1998 18-11-1996 10-08-2000 04-03-1999 31-10-1996 25-03-1998
RU 2086232	A	10-08-1997		NONE		
WO 9952549	A	21-10-1999		AU 3419799 A EP 1069910 A		01-11-1999 24-01-2001
WO 0047222	A	17-08-2000		AT 19499 A AU 2525300 A		15-12-2000 29-08-2000
WO 9417827	A	18-08-1994		AT 195077 T AU 668290 B AU 6106594 A CA 2156084 A DE 69425427 D EP 0682528 A ES 2150982 T JP 9508614 T NO 953182 A US 5942237 A		15-08-2000 26-04-1996 29-08-1994 18-08-1994 07-09-2000 22-11-1995 16-12-2000 02-09-1997 12-10-1995 24-08-1999
WO 9636352	A	21-11-1996		US 5653987 A AU 5642396 A CA 2210996 A EP 0813421 A		05-08-1997 29-11-1996 21-11-1996 29-12-1997